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**BRITISH JOURNAL OF OBSTETRICS AND
GYNAECOLOGY** vol.87, no.9, September
1980, pages 786-796, London GB; C.J.Marvell
et al: "The normal condition of the fetal
electrocardiogram during labor"

JOURNAL OF BIOMEDICAL ENGINEERING
vol.2, July 1980, pages 216-220, Guildford GB;
C.J.Marvell et al: "A simple software routine
for the reproducible processing of the elec-
trocardiogram".

**Econometric Methods (2nd edition);
J.Johnston, pages 32-34**

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Description

The present invention relates to monitoring fetal health during labour.

The present inventors have become aware that changes in that part of the fetal electrocardiogram (FECG) known as the P-R interval (that is the time interval between the peak of the P wave and the R peak - see Figure 3) herald a deterioration in the acid-base status of fetal blood. Previous reports of P-R interval changes have been both infrequent and, in part, contradictory. In papers, dated 1974 and before, and probably based on the analysis of recorded measurements taken during labour, one reported direct correlation between the duration of P-R interval and fetal heart rate (FHR) (although not when there was fetal tachycardia) and another that the P-R interval shortened with decelerating FHR. In another such paper a shortening of the P-R interval with acidosis was noted, while a different paper reported a long-term trend for the P-R interval to diminish towards the end of labour. A shortening or lengthening of the P-R interval with decelerations in FHR late in labour was also separately reported.

According to a first aspect of the present invention there is provided a method of monitoring fetal health during labour comprising the steps of repeatedly deriving a signal representative of the P-R interval of the fetal heart, repeatedly deriving a signal representative of the period of the fetal heart, and repeatedly deriving a signal representative of the relationship between the directions of change of, firstly, the P-R interval and, secondly, the fetal heart rate to provide an indication of fetal health.

According to a second aspect of the invention there is provided apparatus for monitoring fetal health during labour comprising means for repeatedly deriving a signal representative of the P-R interval of the fetal heart, for repeatedly deriving a signal representative of the period of the fetal heart, and for providing an indication of the relationship between directions of change of, firstly, the P-R interval and, secondly, the fetal heart rate to provide an indication of fetal health.

In providing the said indication, the FHR is usually used as the signal representative of the period of the fetal heart.

The said means usually includes a programmed special purpose computer comprising at least one integrated circuit processor, and in both the method and apparatus of the invention the said signals are usually digital signals existing in an operating computer.

Preferably the method of the invention includes deriving an indication of the correlation between the duration of the P-R interval and the FHR or the repetition period of the FECG to provide an indication of the said relationship. Apparatus according to the invention preferably includes means for deriving the said correlation.

The present inventors have found that in a healthy fetus the correlation between the duration of the P-R interval and the FHR is negative but when acidosis, indicating hypoxia, occurs this correlation becomes positive. Thus the inventors have found that the P-R interval may lengthen or shorten with fall in FHR and while the former is an indication of a healthy fetus, the latter indicates probable hypoxia.

However, comparatively short periods, for example 10 minutes, of positive correlation between the duration of the P-R interval and the FHR can occur even in a healthy fetus and for this reason a comparatively long period, for example half an hour, of positive correlation should occur before it is considered that acidosis has occurred. Even then it is believed to be sensible to wait for a significant fall in the elevation of the S-T interval of the FECG before confirming acidosis.

Thus the method of the present invention preferably includes repeatedly measuring the elevation of the S-T interval and similarly the apparatus of the invention preferably also includes means for repeatedly measuring the S-T elevation.

An important advantage of the invention therefore is that a reliable indication of fetal hypoxia is given, it is believed, by the value of the correlation between the FHR and P-R interval when these quantities are measured repeatedly and the correlation is derived on-line. This is particularly true when an on-line indication of the elevation of the S-T interval is also given.

The present inventors believe that the following physiological explanation explains why the method and apparatus of the invention can be used in detecting acidosis. Under normal oxygen supply there is a negative correlation between the P-R interval and heart rate as has been observed in the exercising adult human. Exercise causes adrenalin to rise causing an increase in heart rate and a decrease in the P-R interval. At the beginning of labour respiration is aerobic and a "normal" negative correlation between the FHR and the P-R interval occurs. In the second stage of labour oxygen levels in the blood supplied to the fetus are likely to fall and this causes, as is normal in such circumstances, adrenalin production. As a result the FHR rises and the P-R interval falls. However if the oxygen supply continues to fall so that hypoxia sets in then the fetus switches to anaerobic respiration with the result that the lactic acid is produced and acidosis begins to occur. The low oxygen supply causes the fetal heart rate to drop which as expected

causes adrenalin to be produced by the fetus so that the P-R interval is shortened. However the fetal heart rate is not greatly increased by the high adrenalin level and the expected increase in FHR appears to be overridden by the low oxygen supply. Thus the inverse relationship between FHR and P-R interval is reversed and the fetal heart rate correlates positively with the P-R interval. Results of recorded measurements made from fetal lambs under conditions of partial and complete acute hypoxia suggest that the alteration in the correlation between the FHR and the P-R occurs at a time of lactic acid production.

The coefficient of correlation between the FHR and the P-R interval is known by the inventors as the Conduction Index and from the above discussion the Conduction Index appears to identify those fetuses in which some degree of anaerobic respiration is occurring and, therefore, those fetuses at risk from hypoxia during labour.

Preferably the method (and apparatus) of the invention also includes finding (or means for finding) the conduction index by deriving the Pearson coefficient of correlation as the index. An expression for this coefficient is given later.

As stated, the Pearson coefficient requires the calculation of the correlation coefficient between the P-R interval and the FHR. This can be done instantaneously in real time. Typically, these two quantities are averaged over intervals of about one minute (one minute plus or minus 20 percent), and some ten pairs (ten plus or minus two) are used to calculate the Pearson coefficient. This procedure acts as a form of filtering that eliminates spurious responses whilst retaining sufficient clinical sensitivity. The intervals of time, and number of pairs, can be varied in order to change the sensitivity of the conduction index in responding to changes in fetal distress.

A further advantage of the invention is that if the conduction index is calculated in this way then the quantities required can be obtained without very complicated processing so allowing a reasonably economical monitoring apparatus to be manufactured. Also the conduction index allows a display to be generated which indicates trends without too many variations due to temporary disturbances. Apparatus according to the invention may conveniently display conduction index, S-T elevation, fetal heart rate and inter-uterine pressure (IUP). Although the latter two quantities are being questioned recently as indicators of fetal health, it is believed that they should be displayed to provide continuity with previous instrumentation.

Certain embodiments of the invention will now be described, by way of example, with reference to the accompanying drawings, in which:-

Figure 1 is a block diagram of apparatus according to the invention,

Figure 2 is a flow chart of an algorithm carried out repeatedly by the processor of Figure 1 to determine the conduction index and S-T elevation,

Figure 3 is an example of an enhanced FECG,

Figure 4 shows a reconstruction of conduction index and S-T elevation which occurred during a birth and is given as an example of the type of display which may be given by the apparatus of Figure 1,

Figures 5a and 5b show a flow chart of a preferred alternative algorithm for determining the conduction index and S-T elevation,

Figure 6 shows a linear model of an FECG, and

Figures 7 and 8 are flow charts of the routines of Figure 5b for deriving the P-R interval and conduction index.

In Figure 1 a scalp electrode 10 is connected by way of an isolation amplifier 8 (having a bandwidth between 3 dB points from 0.78 Hz to 250 Hz) to an analogue-to-digital converter 11 and thence to a first-in-first-out memory (FIFO) 9 and a processor system. Only the principal components of the processor system are shown: a processor 12, a random access memory (RAM) 13 and a read only memory (ROM) 14 connected by a data bus 15 and an address bus 16. The processor system also includes an integrated graphic circuit 17 connected to a visual display unit (VDU) 19 by way of wiring 18. Although a single processor is shown and an NEC type NS 32-16 processor can be used it may in some circumstances be convenient to use several processors. Equally the integrated graphics circuit 17 may be replaced by several interconnected integrated circuits.

If required the isolation amplifier 8 may also carry inter-uterine pressure signals from a transducer to a further analogue-to-digital converter (not shown), having an output coupled to the bus 15.

The ROM 14 contains a program which carries out the algorithm of Figure 2, or that of Figures 5a and 5b.

As is well known a filter can be designed which rings, that is provides a high amplitude bi-directional pulse for a short interval when a particular waveform is applied to the filter. Such a filter, which can be in digital or analogue form, is said to be matched to the waveform and is known as a matched filter. In operation, samples of the FECG of a fetus during labour are applied by way of the scalp electrode 10 and the analogue-to-digital converter 11 to the processor 12. Use of the FIFO 9 is optional with the algorithm of

Figure 2. In an operation 21 of Figure 2 the processor runs a digital matched filter subroutine matched to an averaged or standardised FECG derived from many fetuses. As a result the output of the matched filter subroutine contains peak values corresponding to ringing and these peak values correspond to the R peak of Figure 3 which is an example of an FECG waveform enhanced to reduce noise.

5 In an operation 22, the processor 12 derives the interval between the R peaks of succeeding FECG waveforms and in the same operation the value derived is converted to the FHR calculated for one minute. To obtain an average value of FHR, each time the FHR is determined it is added to the previous value until an interval of one minute has elapsed when the total value is read out and the sum reset to zero (operation 23).

10 All FECG samples from the analogue-to-digital converter 11 are stored in a portion of the RAM 13 but when an R peak is detected by ringing, the samples corresponding to the FECG waveform from the beginning of the P wave (about 150 msec before the R peak) to the end of the T wave (about 125 msec after the R peak) are transferred to a buffer portion of the RAM 13, each location in the buffer corresponding to a separate sample and therefore to a separate time in the incoming waveform.

15 That portion of the buffer containing samples corresponding to the P wave can be regarded as a window for averaging the P wave. Each FECG occurring in each one minute interval is transferred to the buffer with the R peaks at the corresponding locations as previous FECGs. The contents of corresponding buffer locations in the window for successive FECGs are added to provide a P wave averaged over one minute (operation 24). A double differential algorithm detects the peak of the averaged P wave (operation 25) and since the location in the buffer which stores the peak of the P wave is now known as is the location containing the R peak, the P-R interval is found simply by subtracting the address of one location from the other in an operation 26.

Averaging the P-R interval and fetal heart rate over one minute as in operations 23 and 24 reduces noise.

20 In an operation 27, the conduction index is obtained by deriving the Pearson correlation coefficient using ten previous values of the average P-R interval and the average FHR, each for one minute as derived in the operations 23 to 26. The expression for the Pearson coefficient is as follows:-

$$\begin{aligned}
 30 \quad r = & \frac{N \sum_{L=1}^N \overline{PR} \cdot \overline{FHR} - \left(\sum_{L=1}^N \overline{PR} \right) \cdot \left(\sum_{L=1}^N \overline{FHR} \right)}{\sqrt{\left\{ N \sum_{L=1}^N \overline{PR}^2 - \left(\sum_{L=1}^N \overline{PR} \right)^2 \right\} \cdot \left\{ N \sum_{L=1}^N \overline{FHR}^2 - \left(\sum_{L=1}^N \overline{FHR} \right)^2 \right\}}} \\
 35
 \end{aligned}$$

where N is the number of FHR and P-R averaged intervals forming a data set within the 10 minute interval.

40 A further series of the buffer locations corresponding to the S-T segment form a window for this segment. Each time an FECG is read into the buffer the contents of these window locations are summed over an interval of one minute (operation 28) and expressed as a percentage of the maximum excursion of the Q-R-S complex (operation 29). The averaging process reduces noise but in order to reduce spurious signals still further the average S-T elevation may be subjected to a Kalman filtering subroutine in an operation 30 (see for example "Use of Optimal Estimation Theory, In particular the Kalman filter, in Data Analysis and Signal Processing", by William S. Cooper, Review of Scientific Instruments, 1986, Volume 57, No. 11, pages 2862-2869; and "An Overview of the Kalman Algorithm" by K.C. Shet and B.V. Rao, Int. Journal of Electronics, 1985, Volume 59, No. 6, pages 657-665).

50 Having determined the correlation index and the S-T elevation, a display of these quantities is generated in an operation 31 by passing appropriate values to the integrated graphic circuit 17 which controls the VDU 19. The display (see Figure 4) shows a histogram of the conduction index and the one minute values of the S-T elevation. In the example shown the conduction index is generally negative for the first five hours and ten minutes of labour but then becomes positive indicating the possibility of acidosis. After a further hour the S-T elevation falls abruptly confirming acidosis in this birth (as was verified later).

55 In the method of Figure 2, the FHR and the P-R interval are each averaged over one minute, but it is believed to be better to detect changes in these parameters from one fetal heart beat to the next. Thus an alternative and preferred method of carrying out the invention is now described in connection with Figures 5a and 5b.

Outputs from the A/D 11 of Figure 1 are stored in the FIFO 9 and an interrupt is generated for the processor 12 every 32 ms. When the processor receives the interrupt, the current instruction is completed before branching to an interrupt service routine in which the processor is immediately disabled from further interrupt. Then 16 samples of raw FECG signal, stored in the first-in-first-out memory, are loaded into an input buffer (generated by software and forming part of the RAM 13) capable of holding four FECG waveforms. An input pointer for the buffer is increased by 16 and thus the pointer points to the position of the next entry to the buffer. However when the pointer reaches the end of the buffer it is reset to the beginning. Having transferred data to the buffer the processor 12 reverts to the main routine which has the flow chart of Figure 5.

The FECG waveform is often buried in background noise and the QRS complex is the only recognisable component. Its detection implies the existence of an FECG waveform in the raw signal. A number of methods can be used for recognising the QRS complex including a simple level detection method and a template matching method. However the preferred method is the use of a matched filter as mentioned above. Spectral analysis of fetal QRS complexes shows that the frequency content is mainly confined to the frequency band 17 to 30 Hz. A matched filter is designed to have a pass band exactly matching the spectrum of the QRS complex and can be realised either by hardware circuitry or software programming. Clearly in the present embodiment the matched filter is by software programming the processor 12. The digital matched filter used comprises a 50 Hz rejection (notch) filter, two 2-pole Butterworth low pass digital recursive filters and two 2-pole Butterworth high pass recursive filters. The 50 Hz rejection filter eliminates interference generated by the mains supply, the 2-pole low pass recursive filters are cascaded together to form a fourth-order filter which rejects high frequency noise above 30 Hz and the two Butterworth high pass filters are cascaded together to limit d.c. drift and reject low frequency noise below 17 Hz. The filter coefficients required for the Butterworth filters can be calculated by implementing the software routine given by M.H. Akroyd in "Digital Filters: Computers in Medicine Series" (Ed. D.W. Hill), Butterworths, 1973. Thus in operation 35 of Figure 5a data is read from the input buffer and used in a matched filter routine 36. If the spectrum of the raw data matches the pass band of the filter routine then the output samples describe a "ringing" output, that is a comparatively high amplitude oscillation which decays after a few cycles. A test 37 for a QRS complex is carried out by testing for digital outputs from the filter routine above a threshold level which indicates "ringing".

When the threshold is exceeded the most recent sample to be used in the matched filter is taken as the R peak of Figure 3 and its position in the input buffer is stored as one of a number of R peak pointers (Operation 38). An FECG waveform or complex is then identified as 100 samples which precede the R peak and 150 samples which follow the peak in the input buffer.

To allow for variations in the signal level of signal reaching the A/D 11, the threshold level for detection of the QRS complex is preferably made variable. For example after setting the initial level at the beginning of monitoring to a convenient value, the threshold level can be varied in accordance with maximum levels in each newly detected QRS complex by subtracting a fixed amount from each new maximum level, the fixed amount being set to a value which is greater than the maximum variation between maximum outputs of two successive QRS complexes. When a sudden drop of signal strength occurs, caused for example by a poor contact between an electrode and the fetal scalp, the threshold may no longer be exceeded. To overcome this problem the threshold level may be decremented when the threshold is not exceeded by a fixed amount until QRS complex detection resumes. However in order to guard against the detection of noise, a minimum threshold level may be provided. Additionally it is preferable that if noise spikes are detected then no adjustment of the threshold level occurs.

In detecting a QRS complex the threshold can be exceeded when a noise burst which has a similar frequency spectrum to a genuine QRS complex occurs. Such noise bursts can occur when the scalp clip of an electrode is disturbed during contractions or examinations of the fetus. A routine 40 discriminates against noise bursts by carrying out three tests on the 250 samples mentioned above and located partly before and partly after an R peak. In the first test the baseline of the FECG waveform is checked for slope. The samples representing the waveform are divided into three groups representing the P section, the QRS section and the T section (see Figure 3). If the difference between the baselines of any pair of sections is larger than half the R to Q height or the R to S height, whichever is the larger, then the FECG waveform is classified as a noisy waveform. In the second test the background noise is checked. In a normal signal the amplitude of the background noise ripples is very small compared with the QRS height but sometimes a large amount of noise is picked up by the electrodes. To calculate noise strength the baselines of the P wave section and the T wave section from the first test are subtracted from each point within the corresponding section. The difference is then summed point by point over the section. If this average is more than a quarter of the QRS height the waveform is again classified as noisy. The third test is useful

when the A/D 11 has been saturated possibly by disturbance of the scalp electrode. A counter in the processor 12 is set to count the number of sample points which have full scale deflection, either maximum or minimum, and if on third of the samples is full scale then the waveform is classified as noisy. When a waveform is classified as noisy a status flag is set and used later for validating FHR derivation and in enhancing the FECG.

In operation 38 the position of the R wave peak in the buffer is located. As mentioned above the input buffer holds four complete FECG waveforms so the interval between two R wave peaks can be calculated from the location of the current peak and the previous peak. The FHR value is then derived from:

$$\text{fetal heart rate} = \frac{30,000}{\text{R-R interval}} \quad \text{beats per minute.}$$

A two part test 42 is then carried out to determine whether the FHR value is genuine since it may have been caused by invalid detection or noise spikes. The two part test comprises a first test in which the FHR value is checked against maximum and minimum allowed values set to 240 and 40 beats per minute respectively. If the first test is satisfied a second test is carried out in which the variation between the current value and the most recent of the three last valid FHR values is examined, the FHR value being rejected if it is more than a predetermined amount different from one of the previous values, the predetermined amount increasing with age of previous value. If the second test is not satisfied, reference is made to the result of the routine 40 and if this routine indicated a waveform which was not noisy a reference FHR value is used as the present value, provided the reference value has not been kept for more than a predetermined number of cycles of FHR calculation. The reference value is that of the most recently validated FHR value (provided it was not detected more than three cycles previously) and the predetermined number of cycles depends on how recently this value was validated: values validated in the last, penultimate, and antepenultimate cycle may be used for three, two and one cycles, respectively.

Depending on the result of the test 42 either the FHR value or a reference value is stored in an FHR buffer or an error byte is stored instead (operations 43 and 44). Since R peaks determined in the operation 38 may not be genuine and may instead belong to noise spikes, a pointer for the input buffer is used to indicate the locations of valid R peaks and is set when an FHR value is entered into the FHR buffer. It is not, of course, set when an error byte is entered in place of an FHR value.

When monitoring begins or after failure to maintain consistent FHR values, it is necessary to establish a genuine FHR value. Three successive calculated FHR values are required for this purpose, the variations between any pair of the values being checked against pre-set ranges. If this test is passed the most recent of the three values is then taken as a genuine reading which can be used as a reference in the second validation test above. Otherwise a further FHR reading is obtained until consistency in the FHR readings is achieved when a reference value is stored.

In raw FECG complexes the P and T waves are often poorly defined due to the presence of background noise. In the present embodiment a moving average technique is performed on successive raw complexes of 250 samples located partly before and partly after an R peak in the input buffer (except those complexes classified as noisy by the routine 40) and provides an enhanced waveform for subsequent processing. In operation 45 each of the most recently located 250 data samples is summed with corresponding samples (in relation to the R peak) of a number of previous sets of 250 samples but the various sets are given weighting factors which decrease with the age of the sample set. Thus as time passes the contribution of each set to the sum becomes smaller. The enhanced waveform is taken as the sum of the weighted waveforms and stored in the RAM 13. Sudden changes in the FECG complex are smoothed out by an averaging effect and will not significantly distort the enhanced waveform. Only changes that last for at least a few fetal heart beats will appear in the enhanced FECG. It is known that the effect of this algorithm on the waveform is the same as passing each sample point of the raw complex through its own time coherent filter continuously, that is through 250 such filters. Time coherent filtering is the process of signal recovery from noise in the closest possible time relationship to the sample being recovered and other techniques may be used.

As mentioned in the paper "A simple software routine for the reproducible processing of the electrocardiogram" by C.J. Marvell and D.I. Kirk, published in the Journal of Biomedical Engineering, 1980, Volume 2, July, pages 216 to 220, there are advantages in generating a linear model of the FECG waveform, including providing an objective assessment of the waveform and good noise rejection. Thus an operation 46 generates a linear model from the stored samples of the enhanced waveform in the way described in the paper by Marvell and Kirk with the result shown in Figure 6 where the model is made up of

a number of intersecting linear segments designated 1' to 14'. The intersections of the lines are known as reference points and the time locations of the reference points are stored in a table in the RAM 13. However, they are first checked to see if they are within acceptable limits and if not an error byte is stored instead.

5 With this model various parameters can be derived including the P-R interval. The P-R interval is derived by a routine 47 shown in Figure 7. A test 51 is carried out to determine whether the P and R time locations as stored in the operation 46 are valid or contain error bytes. If invalid an error byte is stored in a P-R buffer operation 52, but if valid the P-R Interval is calculated by subtracting the time location of the reference point at the intersection of the lines 2' and 3' from that of the reference point at the intersection of the lines 7' and 8' in an operation 53. If, as indicated by a test 54, the P-R buffer contains a previous valid P-R value, the latest value is compared with the most recent stored value (operation 55) and if it is within 5% (operation 56) it is stored in the P-R buffer in an operation 57. If the test 56 is negative, a test 58 is carried out to check whether the test 56 has failed five times already. If so the P-R value is accepted as valid and the operation 57 takes place. If not an error byte is entered in the operation 52.

15 To derive the S-T elevation (operation 48), the height of the isoelectric line is first derived as the average of 10 data points of the enhanced FCG starting from 15 samples before the P wave onset (that is the intersection of lines 1' and 2' in Figure 6). The S-T segment is a short segment after the termination of the S wave (the intersection of lines 9' and 10' in Figure 6) and the onset of the T wave (the intersection of lines 11' and 12'), and the relative height of this segment over the isoelectric line, expressed as the height of the R wave peak to the S wave peak, known as RS(p), or the R wave peak to the Q wave peak, known as RQ(p), is the elevation of the S-T segment which is calculated in an operation 47. Thus the S-T elevation is derived as a percentage from the following equation

$$25 \quad \% \text{ S-T elevation} = \frac{100}{\text{RS(p) or RQ(p)}} \times (\text{av} - \text{iso})$$

where "av" is average of the S-T segment amplitude and is defined as the average of 10 data points of the enhanced FCG starting at 5 data points after the S wave termination, and "iso" is the height of the isoelectric line calculated as described above. Percentage elevations greater than 100% mean the S-T segment is above the isoelectric line, while elevations less than 100% mean the S-T segment is depressed below the isoelectric line.

A routine 49 calculates the conduction index according to the previously given equation for "r" (expressed as a Pearson coefficient), except that the average values of FHR and P-R are replaced by the values found in the operation 41 and from the enhanced waveform and the linear model in the operation 47. The coefficient "r" is calculated every second using values of FHR and P-R stored over the most recent five minute interval. Thus there is a total of 300 points in each calculation (N = 300), except as follows: where FHR or P-R values for a point are invalid as indicated by error bytes, that point is discarded and the total number of points is decremented. When the total falls below 200, the calculation is not completed and an error byte is produced as an indication.

The routine 49 is shown in more detail in Figure 8. Since the conduction index does not immediately become valid once measurements and calculations start, a latency period is allowed before the conduction index is calculated and displayed. A test 60 checks a status flag for the continuation of this period and if it is satisfied, a waiting period 61 of five minutes occurs and then a test 62 is followed by resetting the status flag (operation 63) if the period is over. If the flag is reset at the test 60, a test 64 is made for valid FHR values (in the FHR buffer) and R-R values, and a count of pairs of such values is incremented by one (operation 65), if valid. Otherwise the count is decremented (operation 66) and an error byte entered into a conduction index buffer (operation 67). Following the operations 63 or 65, the number of FHR and R-R pairs are checked (test 68) and if greater than 200, the conduction index is calculated as mentioned above (operation 68) and then the FHR and R-R buffer are updated in an operation 70.

Having derived the correlation coefficient and the S-T elevation, these quantities are displayed on an oscilloscope or by means of a printer, or both, in an operation 50 which is equivalent to the operation 31 of Figure 2.

55 While the invention has been specifically described it will be realised that it can be put into practice in other ways. For example other types of correlation coefficients and values averaged over other time intervals may be used. The processes and apparatus for monitoring fetal health in the general way described may also be varied.

Claims

1. Apparatus for monitoring fetal health during labour comprising means (12 to 19) for repeatedly deriving a signal representative of the P-R interval of the fetal heart and for repeatedly deriving a signal representative of the fetal heart rate, characterised in that the said means is arranged to provide an indication of the relationship between directions of change of, firstly, the P-R interval and, secondly, the fetal heart rate to provide an indication of fetal health.
2. Apparatus according to Claim 1 characterised in that the said means is arranged to repeatedly obtain, in operation, a signal representative of the elevation of the S-T interval of the fetal electrocardiogram.
3. Apparatus according to Claim 2 characterised in that the said means is arranged to determine the elevation of the S-T interval above an isoelectric line, and the said means is arranged to calculate the isoelectric line from digital samples, representing a fetal electrocardiogram, over an interval between the end of the T wave of a fetal electrocardiogram cycle preceding a current such cycle, as represented by the said samples, and the beginning of the P wave of the current cycle, as also represented by the said samples.
4. Apparatus according to Claim 1, 2 or 3 characterised in that the said means is arranged to repeatedly derive, in operation, an indication of the correlation between the P-R interval and the fetal heart rate, whereby the sign of the correlation gives an indication of the said relationship.
5. Apparatus according to Claim 4 characterised in that the said means derives the Pearson correlation coefficient from values representing the P-R interval and values representing the fetal heart rate.
6. Apparatus according to Claim 5 characterised in that the said P-R values and fetal heart rate values are averaged over predetermined intervals of duration in the range 40 to 80 seconds before being used as the values representing the P-R interval and fetal heart rate values to derive the Pearson coefficient.
7. Apparatus according to Claim 6 characterised in that a predetermined number of each of the said average values in the range 8 to 12 is used in deriving the Pearson correlation coefficient.
8. Apparatus according to Claim 2, 3 or 4 characterised in that the said means is arranged to carry out a process of, or equivalent to, time coherent filtering of fetal electrocardiogram values to provide an enhanced representation of the fetal electrocardiogram and the enhanced representation is used in deriving the signal representative of the elevation of the S-T interval and/or the indication of the said correlation.
9. Apparatus according to Claim 8 characterised in that the said means is arranged to receive a succession of sets of digital samples representing a fetal electrocardiogram and the said process is continually carried out by weighting the values of a plurality of the most recent sets with weightings which decrease with the age of the set, and summing corresponding values of the sets relative to the R-wave peak to provide the enhanced representation.
10. Apparatus according to any of Claims 4 to 9 characterised by the inclusion of means (17, 18) for displaying the indication of the correlation as a histogram.
11. Apparatus according to any of Claims 4 to 10 insofar as dependent on Claim 2 characterised by the inclusion of means (17, 18) for displaying the said elevation of the S-T interval.
12. Apparatus according to any preceding claim characterised in that the said means is arranged, in operation, to employ a matched filter algorithm to determine when the R peak of each fetal heart cycle occurs, and to derive the FHR from successive detected R peaks.
13. Apparatus according to Claim 12 characterised in that the said means is arranged, in operation, to employ a periodically occurring temporal window positioned relative to the R peak to sample the P wave of the FECG, and to determine the P peak from the samples obtained.

14. Apparatus according to Claim 12 or 13 characterised in that the said means is arranged, in operation, to employ a periodically occurring temporal window positioned relative to the R peak to sample the T wave of the FECG, and to determine the elevation of the S-T segment from the sampled obtained.
- 5 15. A method of providing data for monitoring fetal health during labour comprising repeatedly deriving (26, 47) a signal representative of the P-R interval of the fetal heart and repeatedly deriving a signal representative of the fetal heart rate (22, 41), characterised by providing an indication (27, 31, 49) of the relationship between directions of change of, firstly, the P-R interval and, secondly, the fetal heart rate to provide an indication of fetal health.
- 10 16. A method according to Claim 15 characterised by repeatedly obtaining a signal representative of the elevation (28, 29, 30, 48) of the S-T interval of the fetal electrocardiogram.
- 15 17. A method according to Claim 16 characterised by determining (48) the elevation of the S-T interval above an isoelectric line, calculating the isoelectric line from digital samples, representing a fetal electrocardiogram, over an interval between the end of the T wave of a fetal electrocardiogram cycle preceding a current such cycle, as represented by the said samples, and the beginning of the P wave of the current cycle, as also represented by the said samples.
- 20 18. A method according to Claim 15, 16 or 17 characterised by repeatedly deriving (27, 49) an indication of the correlation between the P-R interval and the fetal heart rate, whereby the sign of the correlation gives an indication of the said relationship.
- 25 19. A method according to Claim 18 characterised by deriving (27, 49) the Pearson correlation coefficient from values representing the P-R interval and values representing the fetal heart rate.
- 30 20. A method according to Claim 16, 17 or 18 characterised by carrying out a process (45) of, or equivalent to, time coherent filtering of fetal electrocardiogram values to provide an enhanced representation of the fetal electrocardiogram and the enhanced representation is used in deriving the signal representative of the elevation of the S-T interval and/or the indication of the said correlation.
- 35 21. A method according to Claim 20 characterised by receiving a succession of sets of digital samples representing a fetal electrocardiogram and continually carrying out the said process by weighting (45) the values of a plurality of the most recent sets with weightings which decrease with the age of the set, and summing corresponding values of the sets relative to the R-wave peak to provide the enhanced representation.
- 40 22. A method according to any of Claims 18 to 21 characterised by displaying (50) the indication of the correlation as a histogram.
- 45 23. A method according to any of Claims 18 to 22 insofar as dependent on Claim 16 characterised by displaying (50) the said elevation of the S-T interval.
24. A method according to any of Claims 15 to 23 characterised by employing a matched filter algorithm (21, 36) to determine when the R peak of each fetal heart cycle occurs, and to derive the FHR from successive detected R peaks (22, 23, 38, 41).

Patentansprüche

- 50 1. Apparat zur Gesundheitsüberwachung des Fetus während der Wehen, umfassend Mittel (12 bis 19) zur wiederholten Ableitung eines Signals, das das P-R-Intervall des fetalen Herzens darstellt, und zur wiederholten Ableitung eines Signals, das die Herzfrequenz des Fetus darstellt, dadurch gekennzeichnet, daß besagte Mittel Meßergebnisse für das Verhältnis zwischen den Änderungstendenzen des P-R-Intervalls und der Herzfrequenz des Fetus und damit für den Gesundheitszustand des Fetus bereitstellen.
- 55 2. Apparat nach Anspruch 1, dadurch gekennzeichnet, daß besagte Mittel im Betriebszustand wiederholt ein Signal abnehmen, das die Elevation des S-T-Intervalls des Fetus-Elektrokardiogramms darstellt.

3. Apparat nach Anspruch 2, dadurch gekennzeichnet, daß besagte Mittel die Bestimmung der Elevation des S-T-Intervalls über einer isoelektrischen Linie ermöglichen, daß besagte Mittel weiterhin die Berechnung der isoelektrischen Linie nach digitalen Proben, die ein Fetus-Elektrokardiogramm r präsentieren, ermöglichen, wobei das Intervall vom Ende der T-Welle des dem aktuellen FEKG-Zyklus unmittelbar vorausgehenden Zyklus, wie durch besagte Proben dargestellt, zum Beginn der P-Welle des aktuellen Zyklus, wie ebenfalls durch besagte Proben dargestellt, reicht.
4. Apparat nach Anspruch 1, 2 oder 3, dadurch gekennzeichnet, daß besagte Mittel im Betriebszustand wiederholt Angaben zur Korrelation zwischen dem P-R-Intervall und der Fetus-Herzfrequenz ableiten, wobei die Korrelation Rückschlüsse auf besagtes Verhältnis zuläßt.
5. Apparat nach Anspruch 4, dadurch gekennzeichnet, daß besagte Mittel aus Werten für das P-R-Intervall und Werten für die Fetus-Herzfrequenz den Koeffizienten für die Pearson-Korrelation ableiten.
6. Apparat nach Anspruch 5, dadurch gekennzeichnet, daß von besagten P-R-Werten und besagten Werten für die Fetus-Herzfrequenz über vorbestimmte Zeiträume im Bereich zwischen 40 und 80 Sekunden Mittelwerte gebildet werden, die dann als Werte für das P-R-Intervall und die Fetus-Herzfrequenz zur Ableitung des Pearson-Koeffizienten genutzt werden.
7. Apparat nach Anspruch 6, dadurch gekennzeichnet, daß zur Ableitung des Pearson-Koeffizienten eine vorbestimmte Anzahl der besagten Mittelwerte im Bereich von 8 bis 12 verwendet wird.
8. Apparat nach Anspruch 2, 3 oder 4, dadurch gekennzeichnet, daß besagte Mittel eine zeitkohärente Filterung der Werte des Fetus-Elektrokardiogramms oder einen dazu äquivalenten Prozeß durchführen, um eine bereinigte Darstellung des Fetus-Elektrokardiogramms zu erzeugen, wobei diese bereinigte Darstellung des Fetus-Elektrokardiogramms zur Ableitung des Signals für das S-T-Intervall und/oder zur Ableitung von Angaben zu besagter Korrelation verwendet wird.
9. Apparat nach Anspruch 8, dadurch gekennzeichnet, daß besagte Mittel eine Folge von digitalen Werten empfangen, die ein Fetus-Elektrokardiogramm darstellen, und weiterhin dadurch gekennzeichnet, daß besagter Prozeß fortlaufend durch Wichtung der Werte mehrerer der jeweils aktuellsten Wertegruppen durchgeführt wird, wobei der Wichtungsfaktor mit zunehmendem "Alter" der Wertegruppe abnimmt, und daß die entsprechenden Werte der Wertegruppen in bezug auf den Spitzenwert der R-Welle summiert werden, um besagte bereinigte Darstellung zu erzeugen.
10. Apparat nach einem der Ansprüche 4 bis 9, dadurch gekennzeichnet, daß er Mittel (17, 18) einschließt, die eine Ausgabe der Korrelation als Histogramm ermöglichen.
11. Apparat nach einem der Ansprüche 4 bis 10, sofern abhängig von Anspruch 2, dadurch gekennzeichnet, daß er Mittel (17, 18) einschließt, die die Ausgabe besagter Elevation des S-T-Intervalls ermöglichen.
12. Apparat nach einem der vorgenannten Ansprüche, dadurch gekennzeichnet, daß besagte Mittel im Betriebszustand den R-Spitzenwert jedes Herzzyklus des Fetus anhand eines Algorithmus für signalangepaßte Filter zeitlich bestimmt und anhand von aufeinanderfolgenden R-Spitzenwerten die FHR ableitet.
13. Apparat nach Anspruch 12, dadurch gekennzeichnet, daß besagte Mittel im Betriebszustand zur Bestimmung der P-Welle des FEKG und folglich zur Ermittlung des P-Spitzenwertes ein periodisch wiederkehrendes, temporäres Fenster verwenden, das in bezug auf den R-Spitzenwert positioniert wird.
14. Apparat nach Anspruch 12 oder 13, dadurch gekennzeichnet, daß besagte Mittel im Betriebszustand zur Bestimmung der T-Welle des FEKG und folglich zur Ermittlung der Elevation des S-T-Segments ein periodisch wiederkehrendes, temporäres Fenster verwenden, das in bezug auf den R-Spitzenwert positioniert wird.
15. Eine Methode zur Bereitstellung von Daten für die Gesundheitsüberwachung des Fetus während der Wehen, umfassend die wiederholte Abnahme (26, 47) eines Signals, das das P-R-Intervall des fetalen

Herzens darstellt, und die wiederholte Abnahme eines Signals das die Herzfrequenz des Fetus (22, 41) darstellt, dadurch gekennzeichnet, daß sie Meßergebnisse (27, 31, 49) für das Verhältnis zwischen den Änderungstendenzen des P-R-Intervalls und der Herzfrequenz des Fetus und damit Angaben über den Gesundheitszustand des Fetus bereitstellt.

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16. Eine Methode nach Anspruch 15, dadurch gekennzeichnet, daß sie wiederholt ein Signal aufnimmt, das die Elevation (28, 29, 30, 48) des S-T-Intervalls des Elektrokardiogramms für den Fetus darstellt.

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17. Eine Methode nach Anspruch 16, dadurch gekennzeichnet, daß die Elevation des S-T-Intervalls über einer isoelektrischen Linie bestimmt (48) wird, wobei die isoelektrische Linie nach digitalen Proben berechnet wird, die ein Fetus-Elektrokardiogramm darstellen, wobei das Intervall vom Ende der T-Welle des dem aktuellen FEKG-Zyklus unmittelbar vorausgehenden Zyklus, wie durch besagte Proben dargestellt, bis zum Beginn der P-Welle des aktuellen Zyklus, wie ebenfalls durch besagte Proben dargestellt, reicht.

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18. Eine Methode nach Anspruch 15, 16 oder 17, dadurch gekennzeichnet, daß wiederholt Angaben zur Korrelation zwischen dem P-R-Intervall und der Herzfrequenz des Fetus abgeleitet (27, 49) werden, wobei die Korrelation Rückschlüsse auf besagtes Verhältnis zuläßt.

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19. Eine Methode nach Anspruch 18, dadurch gekennzeichnet, daß aus Werten für das P-R-Intervall und Werten für die Herzfrequenz des Fetus der Koeffizient für die Pearson-Korrelation abgeleitet (27, 49) wird.

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20. Eine Methode nach Anspruch 16, 17 oder 18, dadurch gekennzeichnet, daß eine zeitkohärente Filterung der Werte des Fetus-Elektrokardiogramms oder ein dazu äquivalenter Prozeß durchgeführt wird, um eine bereinigte Darstellung des Fetus-Elektrokardiogramms zu erzeugen, wobei diese bereinigte Darstellung des Fetus-Elektrokardiogramms zur Ableitung des Signals für das S-T-Intervall und/oder zur Ableitung von Angaben zu besagter Korrelation verwendet wird.

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21. Eine Methode nach Anspruch 20, dadurch gekennzeichnet, daß eine Folge von digitalen Werten empfangen wird, die ein Fetus-Elektrokardiogramm darstellen, und weiterhin dadurch gekennzeichnet, daß besagter Prozeß fortlaufend durch Wichtung der Werte mehrerer der jeweils aktuellsten Wertegruppen durchgeführt wird, wobei der Wichtungsfaktor mit zunehmendem "Alter" der Wertegruppe abnimmt, und daß die entsprechenden Werte der Wertegruppen in bezug auf den Spitzenwert der R-Welle summiert werden, um besagte bereinigte Darstellung zu erzeugen.

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22. Eine Methode nach einem der Ansprüche 18 bis 21, dadurch gekennzeichnet, daß die Korrelation als Histogramm ausgegeben (50) wird.

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23. Eine Methode nach einem der Ansprüche 18 bis 22, sofern abhängig von Anspruch 2, dadurch gekennzeichnet, daß besagte Elevation des S-T-Intervalls ausgegeben (50) wird.

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24. Eine Methode nach einem der Ansprüche 15 bis 23, dadurch gekennzeichnet, daß der R-Spitzenwert jedes Herzzyklus des Fetus anhand eines Algorithmus für signalangepaßte Filter (21, 36) zeitlich bestimmt und anhand von aufeinanderfolgenden R-Spitzenwerten (22, 23, 38, 41) die FHR abgeleitet wird.

Revendications

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1. Un appareil pour surveiller la santé du fœtus pendant le travail comprenant un moyen (12 à 19) de dériver de façon répétée un signal représentatif de l'intervalle P-R du cœur du fœtus et de dériver de façon répétée un signal représentatif de la fréquence cardiaque fœtale, caractérisé en ce que ce moyen est prévu pour fournir une indication du rapport entre les sens de modification, premièrement d l'intervalle P-R, et deuxièmement, de la fréquence cardiaque fœtale pour donner une indication d la santé du fœtus.

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2. Un appareil selon la Revendication 1 caractérisé en ce que ce moyen est prévu pour obtenir de façon répétée, en fonctionnement, un signal représentatif de l'élévation de l'intervalle S-T de l'électrocardio-

gramme foetal.

3. Un appareil selon la Revendication 2 caractérisé en ce que ce moyen est prévu pour déterminer l'élévation de l'intervalle S-T au-dessus d'une ligne isoélectrique, et que ce moyen est prévu pour calculer la ligne isoélectrique à partir d'échantillons numériques, représentant un électrocardiogramme foetal, sur un intervalle entre la fin de l'onde T d'un cycle d'électrocardiogramme foetal précédant un cycle actuel, représenté par les échantillons, et le début de l'onde P du cycle actuel, également représenté par les échantillons.
4. Un appareil selon la Revendication 1, 2 ou 3 caractérisé en ce que ce moyen est prévu pour calculer de façon répétée, en fonctionnement, une indication de la corrélation entre l'intervalle P-R et la fréquence cardiaque foetale, le signe de la corrélation donnant une indication de ce rapport.
5. Un appareil selon la Revendication 4 caractérisé en ce que ce moyen calcule le coefficient de corrélation de Pearson à partir de valeurs représentant l'intervalle P-R et de valeurs représentant la fréquence cardiaque foetale.
6. Un appareil selon la Revendication 5 caractérisé en ce que les valeurs de P-R et les valeurs de fréquence cardiaque foetale sont moyennées sur des intervalles prédéterminés d'une durée de l'ordre de 40 à 80 secondes avant d'être utilisées comme valeurs représentant les valeurs de l'intervalle P-R et de la fréquence cardiaque foetale pour calculer le coefficient de Pearson.
7. Un appareil selon la Revendication 6 caractérisé en ce qu'un nombre prédéterminé de chacune de ces valeurs moyennes de l'ordre de 8 à 12 est utilisé dans le calcul du coefficient de corrélation de Pearson.
8. Un appareil selon la Revendication 2, 3 ou 4 caractérisé en ce que ce moyen est prévu pour exécuter un processus de, ou équivalent au, filtrage à cohérence de temps de valeurs d'électrocardiogramme foetal pour donner une représentation enrichie de l'électrocardiogramme foetal et que la représentation enrichie est utilisée dans la dérivation du signal représentatif de l'évaluation de l'intervalle S-T et/ou de l'indication de cette corrélation.
9. Un appareil selon la Revendication 8 caractérisé en ce que ce moyen est prévu pour recevoir une succession de jeux d'échantillons numériques représentant un électrocardiogramme foetal et que ce processus se déroule en continu par pondération des valeurs d'une pluralité des jeux les plus récents, la pondération diminuant avec l'âge du jeu, et totalisation des valeurs correspondantes des jeux par rapport au pic de l'onde R pour donner la représentation enrichie.
10. Un appareil selon l'une ou l'autre des Revendications 4 à 9 caractérisé par l'inclusion de moyens (17, 18) pour visualiser l'indication de la corrélation sous la forme d'un histogramme.
11. Un appareil selon l'une ou l'autre des Revendications 4 à 10 dans la mesure où elles sont dépendantes de la Revendication 2 caractérisé par l'inclusion de moyens (17, 18) pour visualiser l'élévation de l'intervalle S-T.
12. Un appareil selon l'une des revendications qui précèdent caractérisé en ce que ce moyen est prévu, en fonctionnement, pour employer un algorithme de filtre adapté pour déterminer à quel moment le pic R de chaque cycle du coeur du fœtus se produit, et calculer la FCF à partir de pics R détectés successifs.
13. Un appareil selon la Revendication 12 caractérisé en ce que ce moyen est prévu, en fonctionnement, pour employer une fenêtre temporelle apparaissant périodiquement et positionnée par rapport au pic R pour échantillonner l'onde P de l'ECGF, et déterminer le pic P à partir des échantillons obtenus.
14. Un appareil selon la Revendication 12 ou 13 caractérisé en ce que ce moyen est prévu, en fonctionnement, pour employer une fenêtre temporelle apparaissant périodiquement et positionnée par rapport au pic R pour échantillonner l'onde T de l'ECGF, et déterminer l'élévation du segment S-T à partir des échantillons obtenus.

15. Une méthode de fourniture de données pour surveiller la santé foetale pendant le travail consistant à dériver de façon répétée (26, 47) un signal représentatif de l'intervalle P-R du coeur du fœtus et à dériver de façon répétée un signal représentatif de la fréquence cardiaque foetale (22, 41), caractérisé en ce qu'il fournit une indication (27, 31, 49) du rapport entre les sens de modification, premièrement, de l'intervalle P-R, et deuxièmement, de la fréquence cardiaque foetale pour donner une indication de la santé du fœtus.
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16. Une méthode selon la Revendication 15 caractérisée par l'obtention de façon répétée d'un signal représentatif de l'élévation (28, 29, 30, 48) de l'intervalle S-T de l'électrocardiogramme foetal.
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17. Une méthode selon la Revendication 16 caractérisée par la détermination (48) de l'élévation de l'intervalle S-T au-dessus d'une ligne isoélectrique, le calcul de la ligne isoélectrique à partir d'échantillons numériques, représentant un électrocardiogramme foetal, sur un intervalle entre la fin de l'onde T d'un cycle d'électrocardiogramme foetal précédant un cycle actuel, représenté par ces échantillons, et le début de l'onde P du cycle actuel, également représenté par ces échantillons.
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18. Une méthode selon la Revendication 15, 16 ou 17 caractérisée par calcul répété (27, 49) d'une indication de la corrélation entre l'intervalle P-R et la fréquence cardiaque foetale, le signe de la corrélation donnant une indication de ce rapport.
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19. Une méthode selon la Revendication 18 caractérisée par le calcul (27, 49) du coefficient de corrélation de Pearson à partir de valeurs représentant l'intervalle P-R et de valeurs représentant la fréquence cardiaque foetale.
20. Une méthode selon la Revendication 16, 17 ou 18 caractérisée par l'exécution d'un processus (45) de, ou équivalent au, filtrage à cohérence de temps de valeurs d'électrocardiogramme foetal pour donner une représentation enrichie de l'électrocardiogramme foetal et la représentation enrichie est utilisée dans la dérivation du signal représentatif de l'élévation de; l'intervalle S-T et/ou l'indication de cette corrélation.
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21. Une méthode selon la Revendication 20 caractérisée par la réception d'une succession de jeux d'échantillons numériques représentant un électrocardiogramme foetal et le déroulement continu de ce processus par pondération (45) des valeurs d'une pluralité des jeux les plus récents, la pondération diminuant avec l'âge du jeu, et totalisation des valeurs correspondantes des jeux par rapport à la pointe de l'onde R pour donner la représentation enrichie.
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22. Une méthode selon l'une ou l'autre des Revendications 18 à 21 caractérisée par la visualisation (50) de l'indication de la corrélation sous la forme d'un histogramme.
23. Une méthode selon l'une ou l'autre des Revendications 18 à 22 dans la mesure où elles sont dépendantes de la Revendication 16 caractérisée par la visualisation (50) de l'élévation de l'intervalle S-T.
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24. Une méthode selon l'une ou l'autre des Revendications 15 à 23 caractérisée par l'emploi d'un algorithme de filtre adapté (21, 36) pour déterminer le moment où le pic R de chaque cycle du coeur du fœtus se produit, et calculer la FCF à partir de pics R détectés successifs (22, 23, 38, 41).
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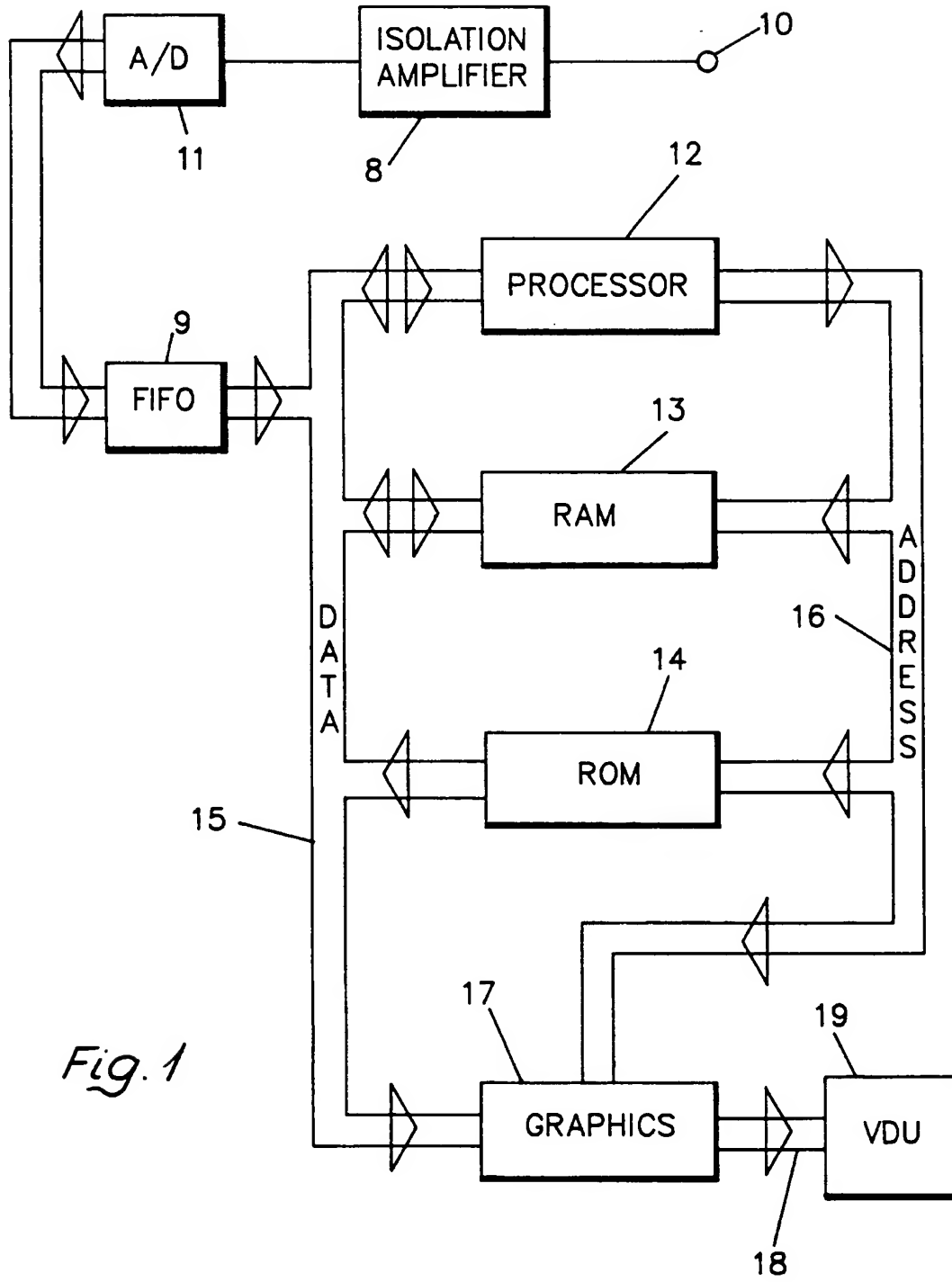
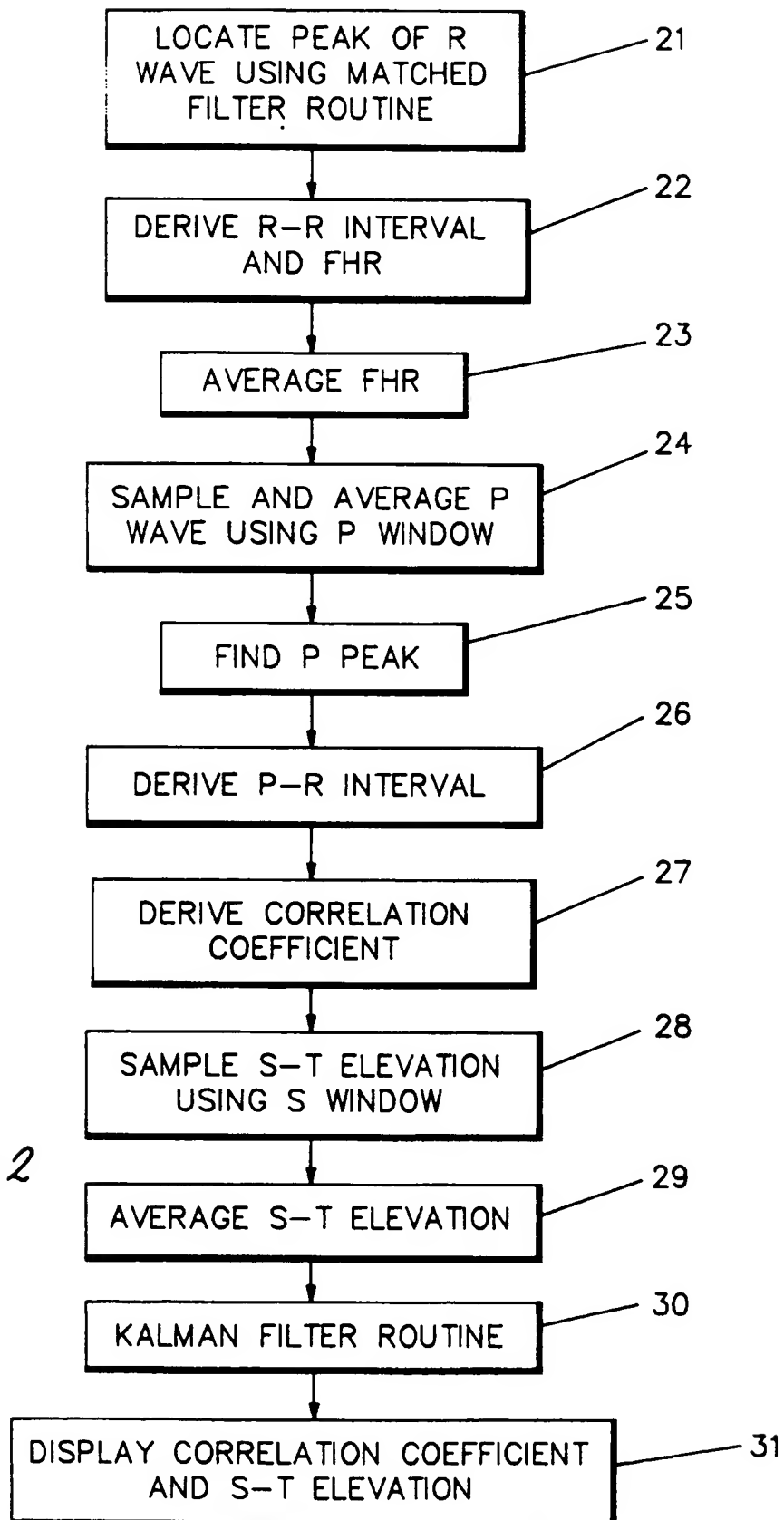


Fig. 1

*Fig. 2*

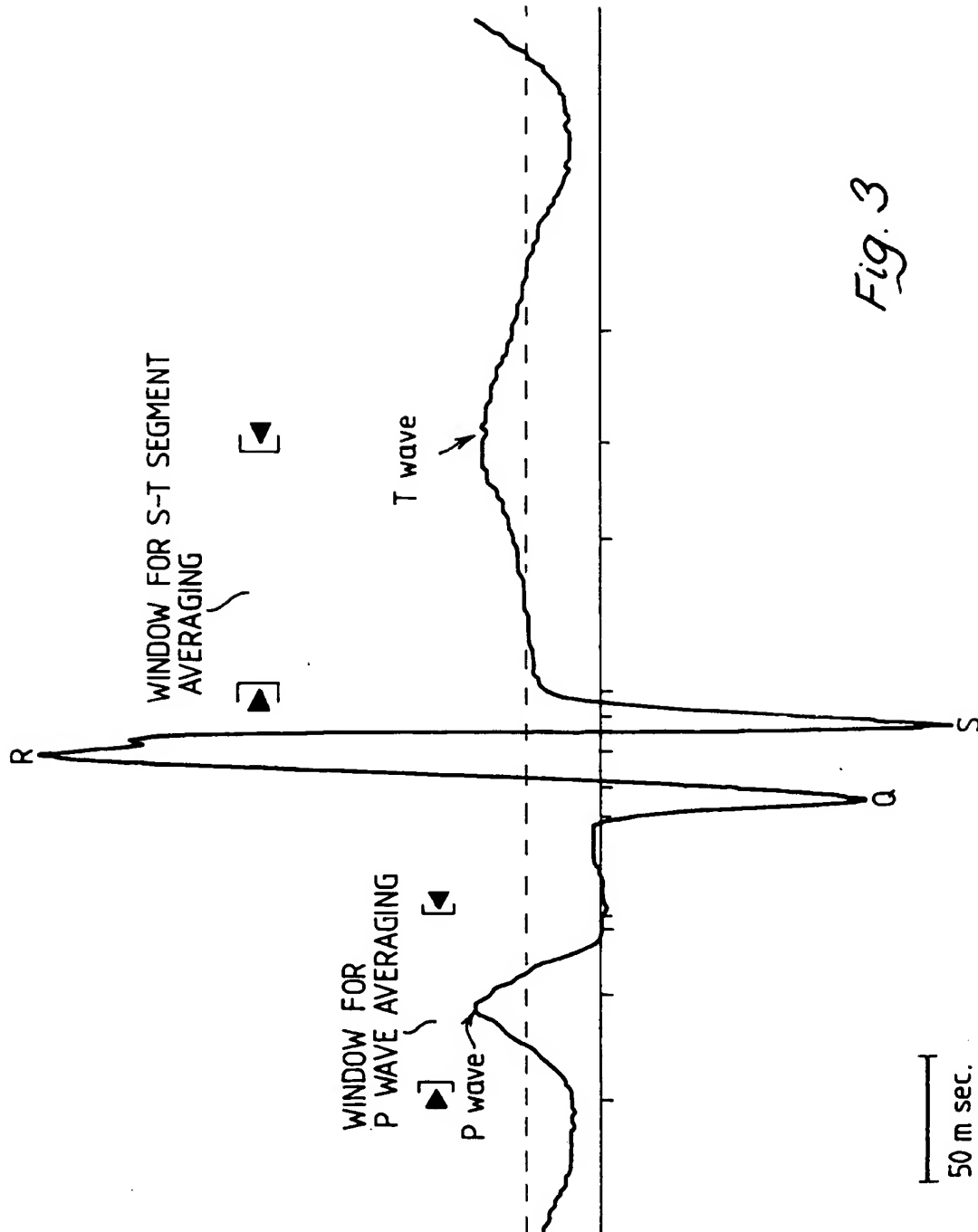


Fig. 3

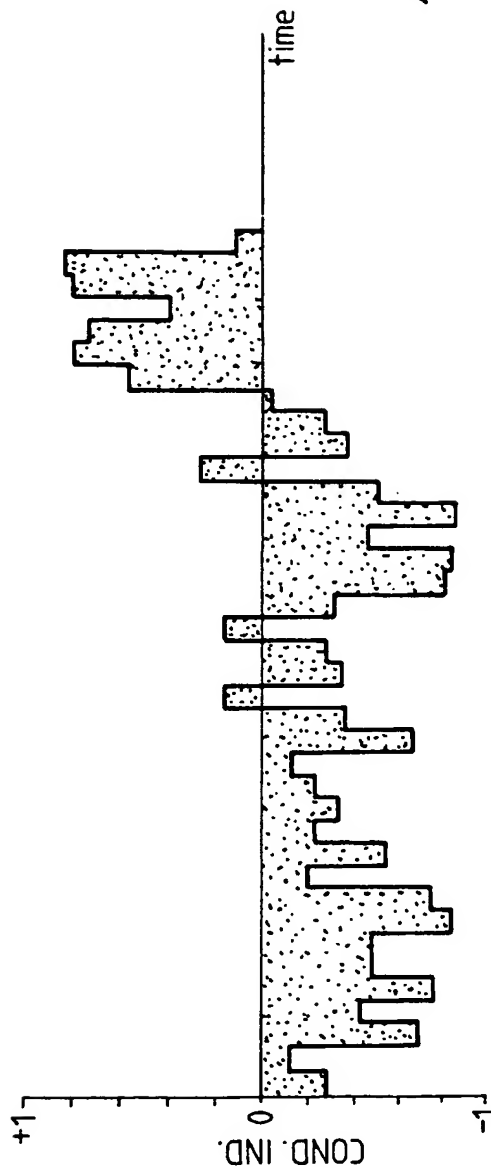
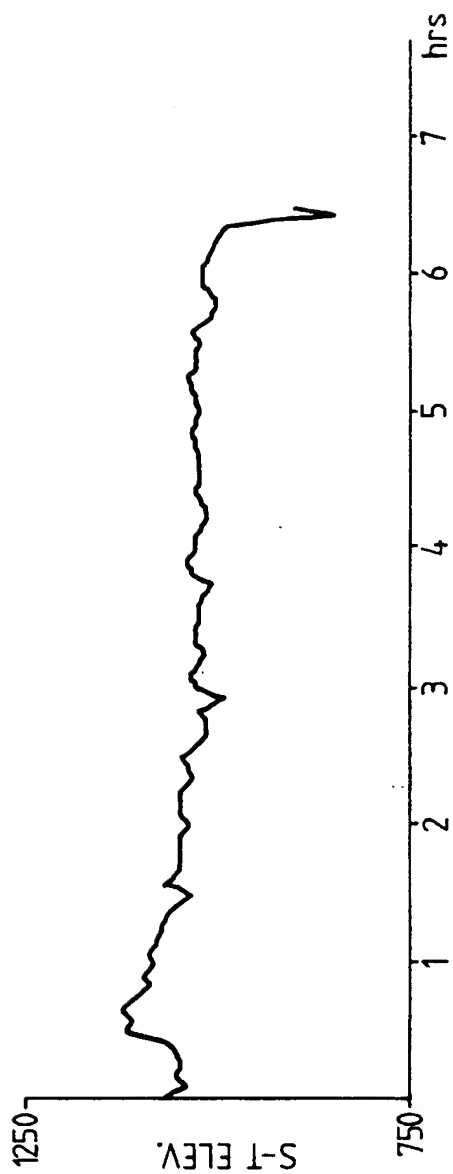
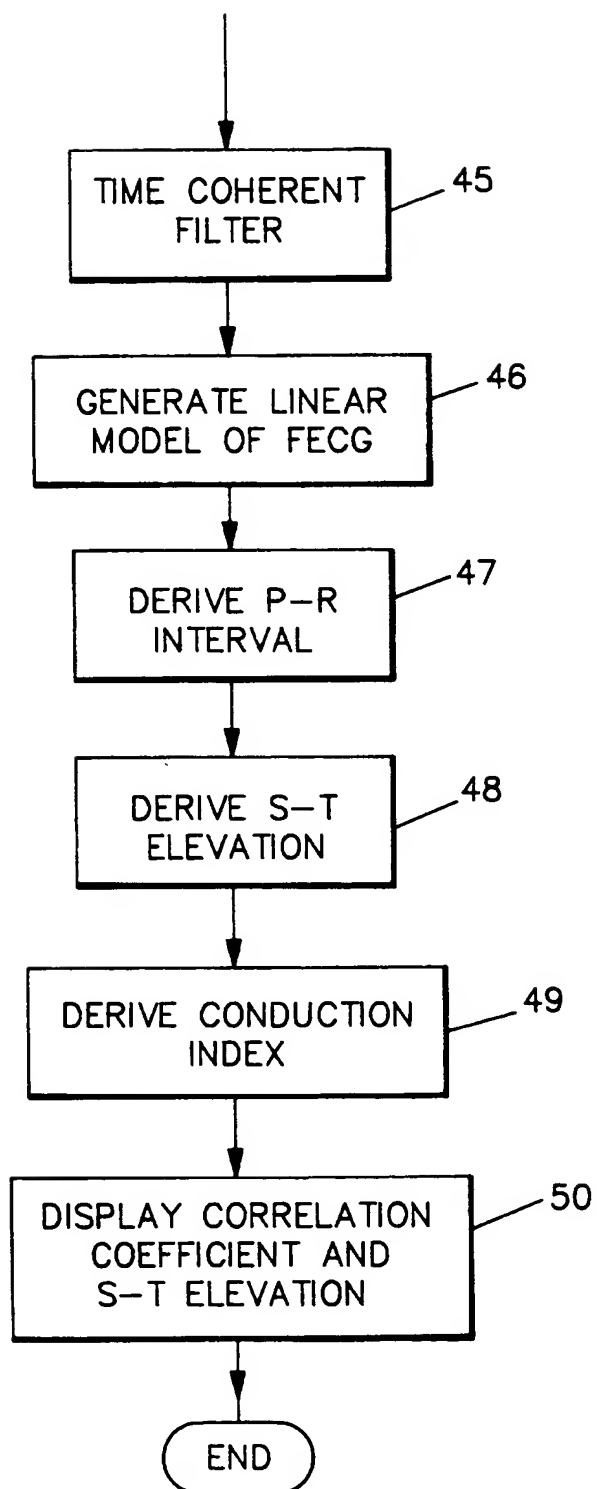
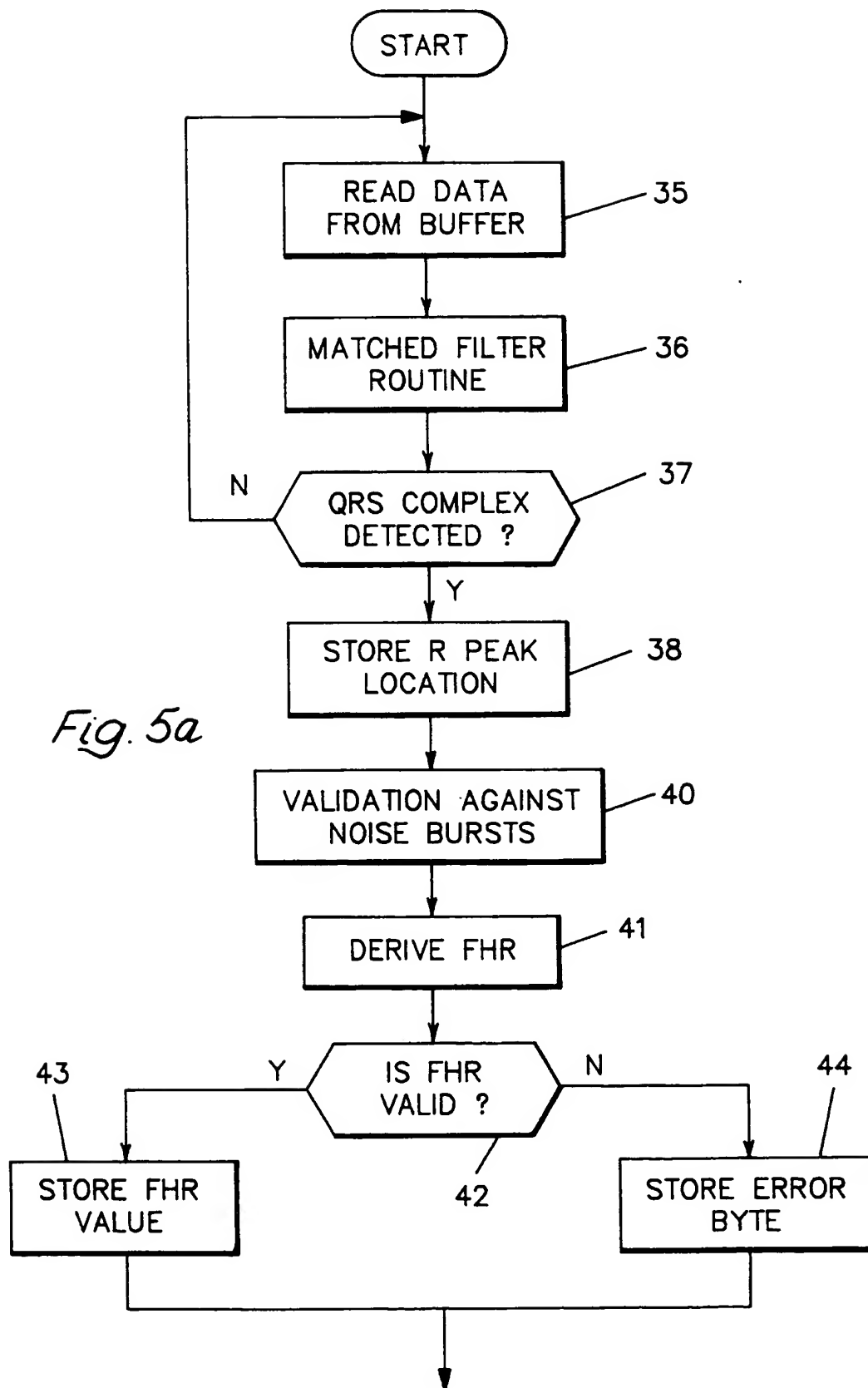


Fig. 4

Fig. 5b





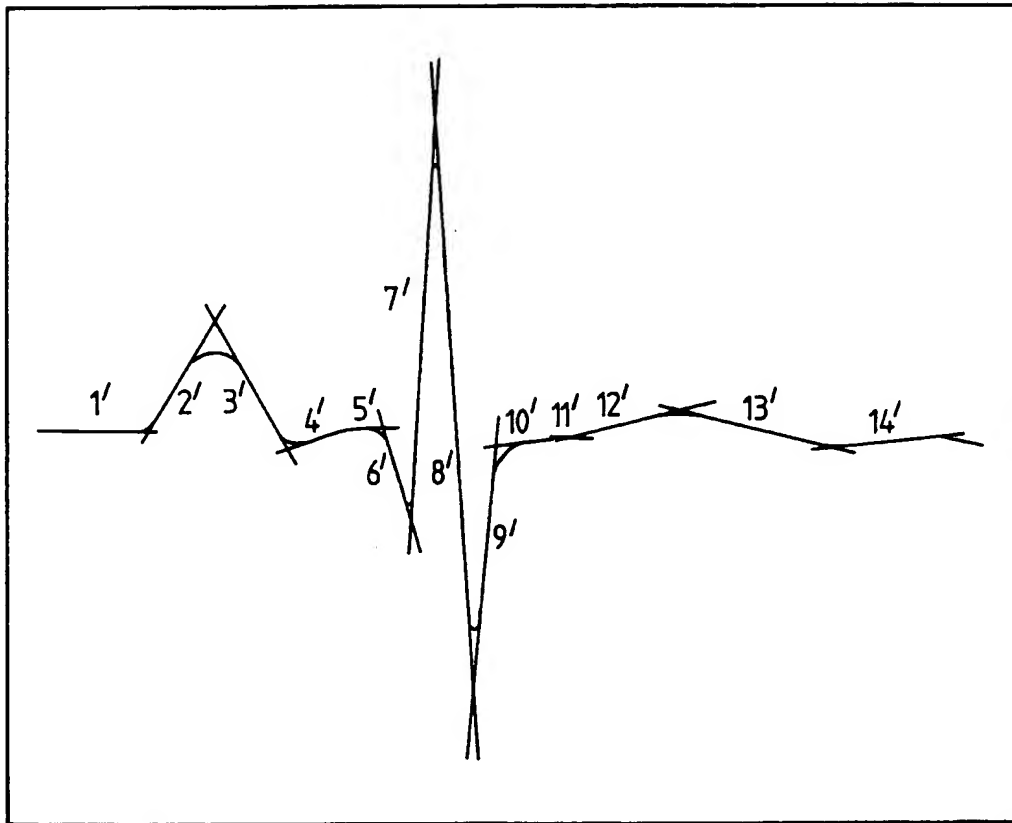


Fig. 6

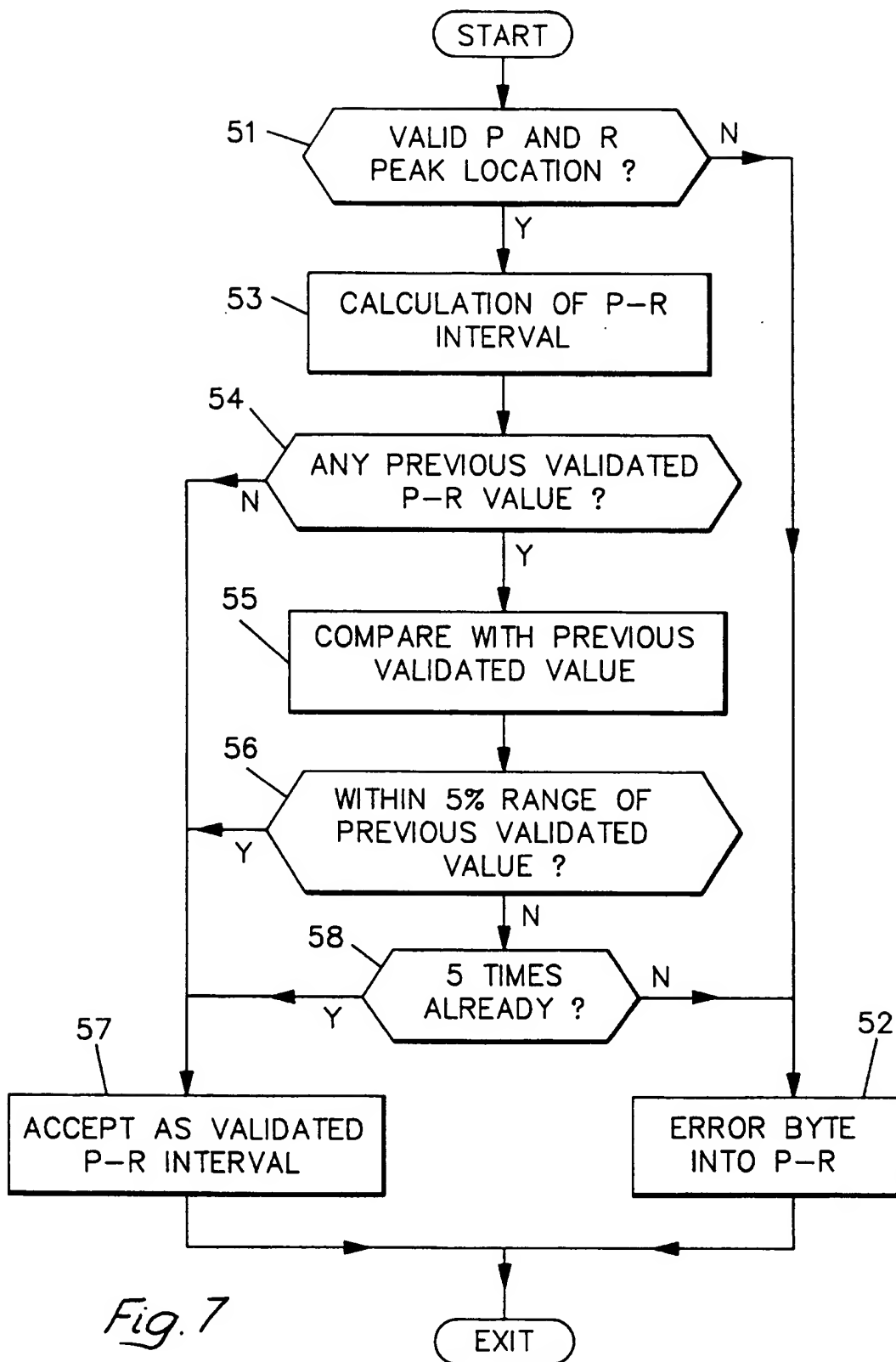


Fig. 7

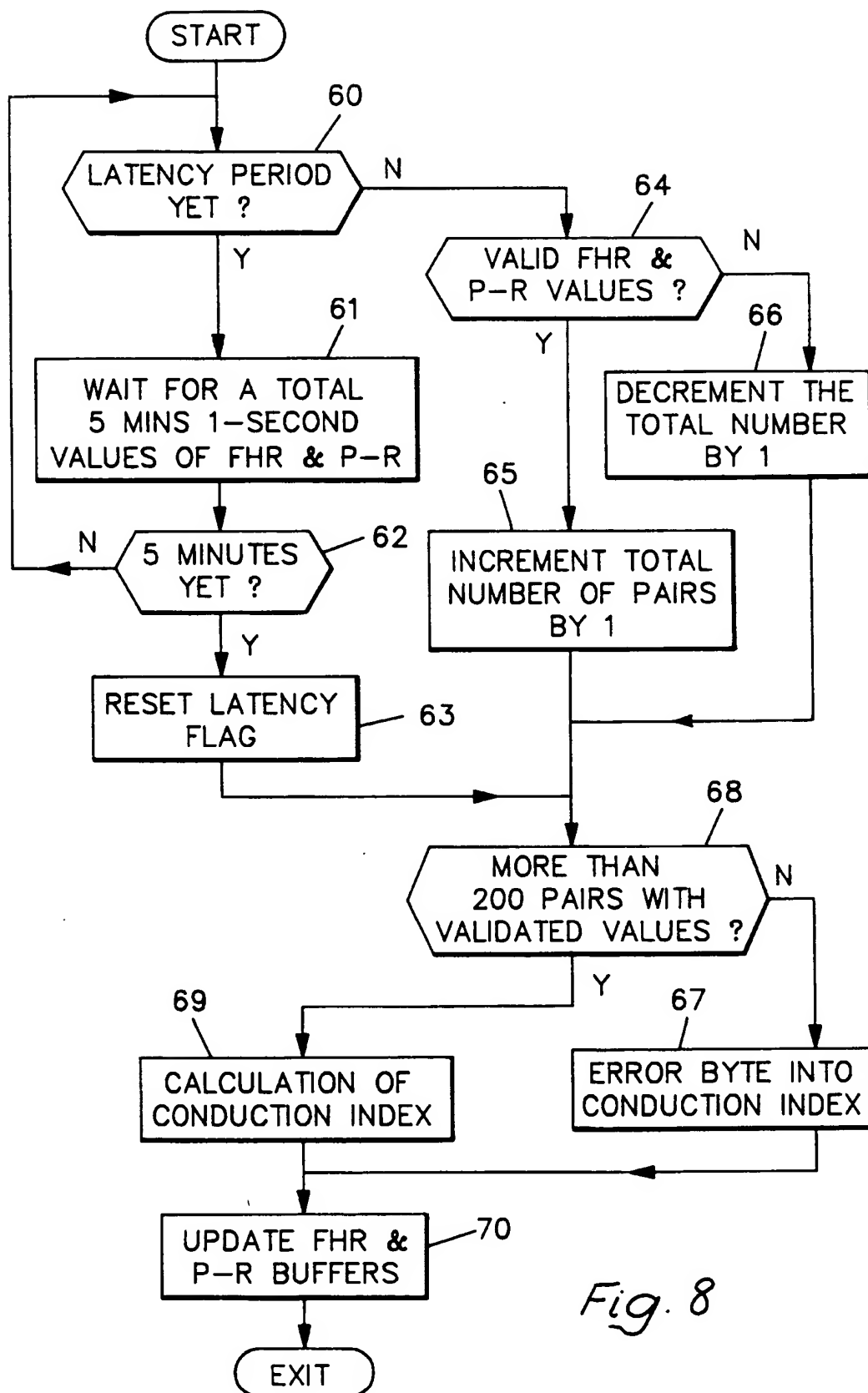


Fig. 8